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a Nordic Lymphoma Group population-based study

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Letter to the Editor

Six cycles of R-CHOP-21 are not inferior to eight cycles for treatment of diffuse large B-cell lymphoma - A Nordic Lymphoma Group population-based study

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The majority of randomised clinical trials that have established R-CHOP-21 as the current

standard treatment for adult patients with diffuse large B-cell lymphoma (DLBCL) have applied eight cycles of chemotherapy [1-3]. Despite a lack of solid evidence to support the use of six instead of eight cycles of R-CHOP-21, six cycles are commonly assigned in clinical routine and endorsed in guidelines.

No randomised trial has demonstrated superiority of eight compared to six cycles of R-CHOP-21. Therefore, we examined whether the use of six versus eight cycles of R-CHOP-21 had impact on survival probability, using data from the Danish and Swedish lymphoma registries, as previously described [4].

This study includes 1170 adult patients diagnosed with DLBCL 2007-2014 in Sweden and Denmark, who received treatment with six or eight cycles of R-CHOP-21. Of these, 1013 (87%) were administered six cycles, and 157 (13%) received eight cycles. Median follow-up time was 5.0 years (range 1.2-9.4).

Reflecting the population-based setting, patient characteristics in the two treatment groups slightly differed, and were marginally inferior in the cohort treated with eight cycles of R-CHOP-21. In survival estimates, crude five-year overall survival (OS) rates were similar for patients treated with six and eight cycles of R-CHOP-21; 74% (95% CI: 71-77%) and 72% (95% CI: 63-79%), respectively (Figure 1). Further, in a multivariate Cox model adjusting for IPI variables and gender, eight cycles of R-CHOP-21 was not associated with better outcome than six cycles (HR: 0.92, 95% CI: 0.66-1.29, $P=0.63$).

To further adjust for imbalances in prognostic factors, a matched sample analysis was performed. Here, the 157 patients who received eight cycles were compared to 157 patients who received six cycles of chemotherapy, matched according to IPI variables and bulky disease. Similar five-year OS of 72% (95% CI: 63-79%) and 76% (95% CI: 67-83%) were observed in the cohort treated with eight and six cycles, respectively. Consistently, no

evidence of a difference was observed in a multivariate analysis (HR with six cycles: 0.88 (95% CI: 0.54-1.44), $P=0.62$).

Additionally, no evidence of a difference in outcome according to use of six or eight cycles of R-CHOP-21 were observed in subgroup analyses stratified according to age $\leq/\geq 70$, low and high-risk IPI score, and excluding patients treated with consolidative radiotherapy.

These results are in line with results from the ECOG/CALGB 9703 study, where the outcome of patients who received six cycles of R-CHOP-21 were comparable to those of patients with similar patient characteristics treated with eight cycles in the GELA study [1, 2].

The RICOVER-60 trial demonstrated increased toxicity in absence of improved outcome with eight compared to six cycles of R-CHOP-14 [5]. However, only elderly patients (aged 60-80) were included and a similar comparison of R-CHOP-21 has not been performed. Thus, the present study contributes valuable data regarding the use of six cycles of R-CHOP-21 among patients of all ages and risk groups.

In summary, we note that the majority of patients with DLBCL treated with R-CHOP-21 during the surveyed time period received six cycles, and conclude that outcomes following six or eight cycles of R-CHOP-21 for newly diagnosed DLBCL are comparable in terms of efficacy.

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Figure 1: Overall survival for patients treated with 6 (red line) and 8 (green line) cycles of R-CHOP-21.

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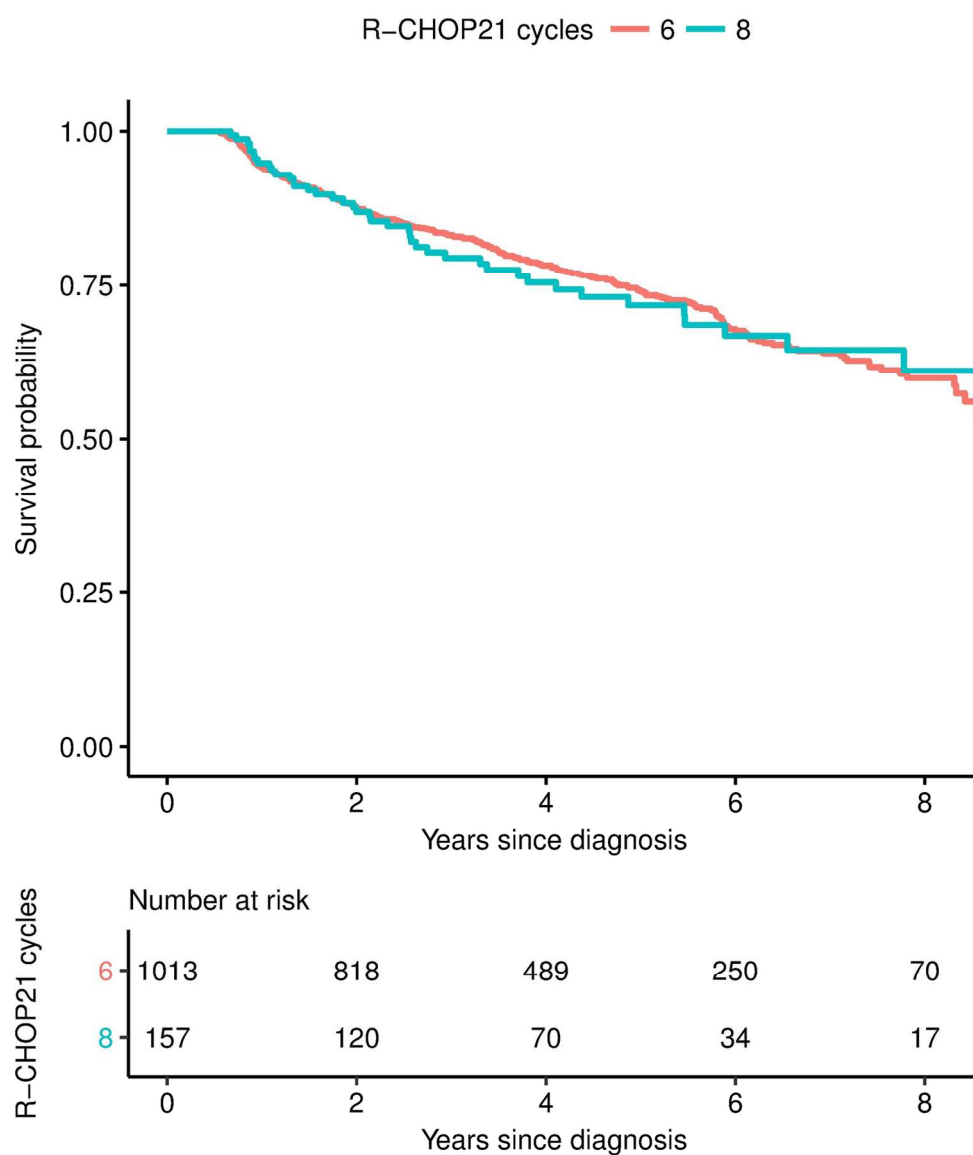


Figure 1: Overall survival for patients treated with 6 (red line) and 8 (green line) cycles of R-CHOP-21.

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